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ORIGINAL ARTICLE

Differential diagnoses of nocturnal fear and movement paroxysm: a case report

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Abstract Recurrent nocturnal behavioural and movement paroxysms are a diagnostic challenge for the clinical pediatrician. We report on an adolescent girl who presents recurrent stereotypical nightmare-like episodes occurring during non-REM sleep stages 1–2 (N1 and N2). We discuss the differential diagnoses between epileptic and nonepileptic events and between nocturnal frontal and temporal seizures. The pathophysiological and unusual electroencephalographical features are discussed with respect to clinical features and results of interictal FDG-PET. *Conclusion* In case of stereotypical nightmare-like episodes in children or adolescents, an epileptic origin has to be ruled out before a parasomnia is diagnosed. In addition, a normal awake EEG or interictal sleep EEG in the diagnostic workup may not exclude an epileptic disorder. In case of nightly stereotypic motor or affective events, an epileptic disorder should be discussed.

Keywords Nocturnal paroxysm · Nocturnal seizures · Ictal fear · Interictal FDG-PET · Pavor nocturnus · Nocturnal panic attacks · Nightmares · Affective epileptic seizures · Autosomal-dominant nocturnal frontal lobe epilepsy

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Introduction

Sleep disorders are one of the most prevalent health problems in the general childhood population. Over 80% of preschool-aged children and 15% of preadolescents suffer from parasomnia events [1, 14]. For the clinical pediatrician and for the sleep specialist, the differentiation between the several paroxysmal events out of sleep, especially the differentiation between sleep disorders (which are recently listed in by Vendrame and Kothare [29]) and nocturnal seizures, is a practical challenge.

Paroxysmal attacks, especially if associated with movement and emotional behavior disorders, may be difficult to differentiate from seizures. This is especially valid in non-REM sleep disorders because the main non-REM sleep arousal disorders, such as confusional arousal or sleep terrors, show a semiological overlap with nocturnal seizures, mainly with nocturnal frontal lobe epilepsy. However, from the viewpoint of an epileptic disorder, it is remarkable that not only frontal lobe seizures but also temporal seizures can mimic parasomnia.

With our case study, first we discuss the practice relevant to the differential diagnosis of parasomnia, nocturnal panic attacks, and seizures in adolescents, and second we discuss different types of nocturnal seizures and unusual ictal electroencephalographic features.

Case study

We report on a 14-year-old girl suffering from first-time episodes of recurrent nightmares during sleep. Family history and personal history is uneventful with respect to sleep disorders or seizures. Two weeks after visiting a ski camp with her class, she presented stereotypical nightmare-like attacks shortly after falling asleep. These episodes were

Table 1 Clinical and electroencephalographic features in differential diagnosis between several parasomnias and nocturnal seizures

	Pavor nocturnus	Nightmares	Nocturnal panic attacks	Affective epileptic seizures	ADN frontal lobe epilepsy
Age at onset (years)	4–12	All age groups[a]	Adolescence and older[a]	All age groups[a]	All age groups (mean age at first seizure 14 years)[a]
Family history of parasomnia	Frequently positive	Frequently negative[a]	Frequently negative[a]	Frequently negative[a]	Sometimes positive
Family history of epilepsy	Negative[a]	Negative[a]	Negative[a]	Sometimes positive	Frequently positive
Spontaneous course	Tend to disappear	Tend to disappear	Stabile with respect to psychological status[a]	Stabile, if not treated[a]	Stabile, if not treated[a]
Sleep stage onset of episodes	Non-REM sleep (first third of night, sw-sleep)[a]	REM sleep (second half of night)	Non-REM sleep (early sleep phase)[a]	Non-REM sleep (shortly after falling asleep)[a]	Non-REM sleep (light sleep)[a]
Triggering factors	None, sometimes sleep deprivation	Stress, traumatic events	Possible	Possible, but not definitely	Possible, but not definitely
Episode frequency	Usually 1–2/night	Usually 1/night	Usually 1/night (often associated with daytime panic attacks)	One to several/night[a]	Usually several/night (often in clusters)[a]
Episode duration	1–15 min	1–30 min	2–8 min[a]	Short, 1 to a few minutes[a]	Seconds up to a few minutes
Stereotypic motor pattern	None	None	None, affective features dominant	Yes, but affective features dominant[a]	Yes[a]
Autonomic discharges	+	+	+++[a]	+++[a]	++
Consciousness after event	Normal if awake, mostly if not fully awake	Normal if awake	Normal, awake during the event	Shortly reduced if awake[a]	Normal if awake
Recall of episodes	Amnesia	Full recall	Full recall	Amnesia or confused memory (feeling of choking is dominant)[a]	Amnesia or confused memory[a]
EEG	Normal, ictal arousal features	Normal	Normal	Abnormal[a]	Abnormal in some cases[a]
Sum of points in differential diagnosis	2	3	7	11[a]	7

[a] Feature, which is fulfilled in our case

observed during night sleep and during afternoon naps. The episodes uniformly started with a motor discomposure. Thereafter she showed rhythmic head and trunk movements from one side to the other, expressing fear and fright on her face while snivelling and shouting. Her hands seemed to be cramped but no tonic or clonic features nor focal signs were witnessed. These episodes lasted 3 to 5 min and could be disrupted by waking her. The episodes occurred repeatedly during one night and could be observed every time she fell asleep. Upon awaking, she recalled her dream as diffusely seeing herself with bloody skin located at trunk, arms, or legs. After a certain amount of time, she developed an anxiety to falling asleep and her sleep quality was less restorative thus causing increased tiredness and sleepiness during daytime. No attacks were observed during the daytime. A neurological examination was completely normal including mental and neuropsychological status. The possibility of psychological trauma during her time at the ski camp, thus causing her panic attacks, was intensively discussed and investigated, although no specific theory existed about what could have happened to the girl during the ski camp.

A normal background activity in EEG during wakefulness was registered. Some sharp wave complexes and dysrhythmic groups were generated on the right and the left sides, without any clear focus (Fig. 1a–b). After falling asleep, some sharp wave complexes frontotemporal left-sided were registered (Fig. 1c). After a short time during non-REM sleep stages 1 and 2 (N1 and N2), clinical signs as mentioned above appeared, while the EEG showed a primary generalized fast rhythmic alpha activity without focal signs, neither at the beginning nor at the end of the episodes (Fig. 1d). No postictal slowing was registered.

The brain MRI with 1-mm slides was normal. However, interictal ^{18}F-FDG positron emission tomography revealed a focal hypometabolic area in the left-sided hippocampus (Fig. 2; for Methods [12, 13]).

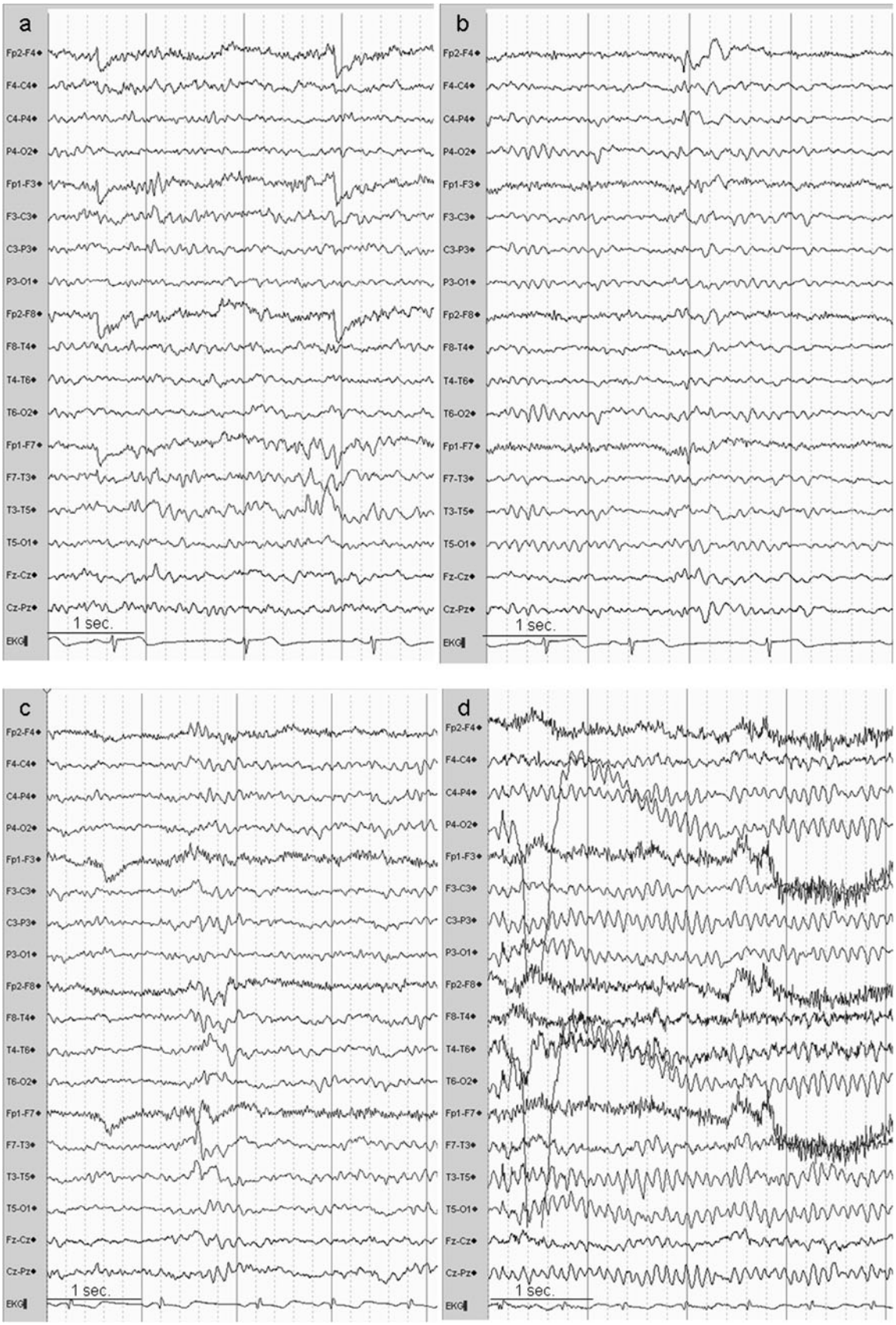

Fig. 1 **a**–**b** EEG in awake stage with some sharp waves (**a**) at the left temporal and (**b**) right fronto-centro-parietal leads (7 μV/mm). **c**–**d** EEG in sleep stage 1 at the beginning (**c**) and during the complex seizure (**d**) (7 μV/mm)

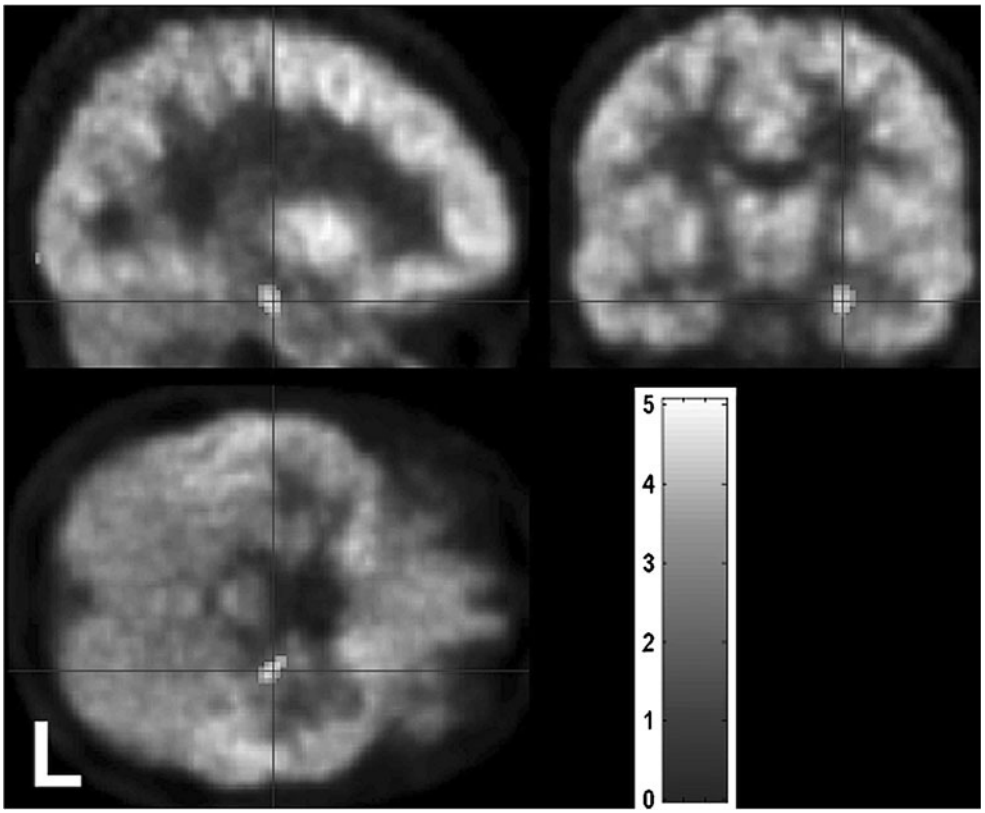

Fig. 2 Maximum intensity projections (MIP) of *Z*-scores of significantly hypometabolic areas ($p<0.05$, corrected for multiple comparisons) comparing the individual patient versus an adult control group, projected on multiplanar reconstructions of the interictal 18-FDG-PET examination (Siemens Biograph 40 TrueV PET/CT). Note circumscribed focal hypometabolism in left hippocampal area

With respect to the generalized ictal EEG and focal findings in FDG-PET, an epileptic cause of the attacks was discussed and a treatment with Lamotrigine was started. The seizures stopped immediately after beginning the prescription dosage of 200 mg/day. After 3 months, the dose was increased to 250 mg/day in order to prevent further abortive seizures.

After 1 year the girl showed a reduced compliance for intake of the antiepileptic drug. At this time, the episodes started again in the same stereotypical fashion as initially observed. In addition, the same interictal and ictal EEG features were generated. In actuality, for the past year and a half, the girl remains seizure-free.

Discussion

The distinction between non-REM parasomnia, nocturnal panic attacks, and nocturnal seizures are, in practice, a significant challenge for the pediatrician. Considering the major features helping to differentiate between these nocturnal episodes, as listed recently by Vendrame et al. [29] and Tinuper et al. [27], our patient displayed mostly the clinical signs of nocturnal seizures (Table 1).

First, we have to differentiate the episodes from non-REM parasomnia. The girl showed more than three episodes per night, which occurred shortly after falling asleep during sleep stages 1 and 2, lasted less than 30 min, were associated with stereotypical movements, and had no verbal interaction. Postictal confusion was absent as was a positive family history for parasomnias, which is considered to be a leading clinical feature of nonepileptic paroxysmal nocturnal events. However, missing a phase of postictal confusion is not an exclusion criterion of nightly seizures (see Table 2). The appearance of confusion is dependent on the type of seizure and the level of reduced consciousness, which is much more intensive in non-REM sleep than in REM sleep. However, the recall of the dream is missing or more confused in the case of a seizure. Ictal episodes out of non-REM sleep are, in part, recalled. Furthermore, the episodes show a high stereotypical pattern of movements and affective features, which is typical for seizures [27].

Second, the fearful symptoms require a differentiation from nightmares. Nightmares are parasomnias which are characterized by an occurrence usually once a night during the second half or last third of the sleep time, missing stereotypic movements, and mainly by strong association to REM sleep stage, features which are missing in our patient.

Third, the occurrence of sleep-associated fearful attacks requires a differentiation from nocturnal panic attacks. In contrast to nocturnal seizures and the semiology of the attacks in our patient, nocturnal panic attacks are characterized by a longer duration of the episodes, missing of predominantly motor features, and a history of daytime attacks. In addition, the attacks are associated with stage 2 of sleep or slow wave sleep. Furthermore, patients are aware during the attacks. Usually,

Table 2 Clinical and electroencephalographic red flags for events out of sleep in children and adolescents which help to avoid a misdiagnosis between seizures and parasomnia

Suggested features for seizures:
• >3 episodes/night and/or <10 episodes/month
• The events frequently occur in clusters
• Episodes occur anytime during the night, primarily during non-REM sleep, some seizures predominantly occur during sleep stages N1/N2
• Episodes are mostly short (from 1 up to a few minutes)
• Motor or affective pattern is stereotypic
• Confused recall of the events
• Daytime tiredness
CAVE: nocturnal seizures are not excluded
• By a normal waking or interictal sleep EEG
• By a (partial, sometimes confused) recall of the events
Suggested features for parasomnias:
• Occurrence during first third of sleep
• Motor and affective patterns are variable
• Complete recall of episodes after awaking (for REM sleep episodes)
• Duration of >10 min
• Tend to disappear with time
• Positive family history
CAVE: parasomnias are not excluded
• By amnesia after awaking (i.e., pavor nocturnus)

patients remember the event, but recall of the episode is also possible in nocturnal frontal lobe seizures [27].

In addition, our patient showed, along with mild unspecific sharp waves in EEG, unusual stereotypic electroencephalographic features during the attacks with fast generalized alpha activity without preceding electroencephalographic arousal features.

The spectrum of epilepsy syndromes in children and adolescents with sleep-associated increase of seizures is large [29]. Nocturnal hyperkinetic seizures are observed in frontal lobe and in temporal lobe epilepsy, especially if the epileptic zone is frontopolar located. On the other hand, fearful experience is also a known feature of medial temporal lobe epilepsy. In most cases fear occurs as an early ictal behavioral manifestation, when the focal area starts to become active [2]. Both amygdalae are involved in generating fearful emotions, although the right one is involved in processing fast, brief, and automatic fear, whereas the left amygdala is active in more detail-oriented and perceptual aspects of the fear. Therefore, it is not surprising that fear, as an epileptic aura symptom, is more often but not exclusively generated in right-sided epileptic activity [9]. Most cases associated with ictal fear present fearful symptoms in an awake state. However, up to 10% of patients with temporal lobe epilepsy present ictal nightmare-like symptoms [23] usually during non-REM sleep stages 1–2. In the study by Vaugier et al. [28], the epileptogenic zone in patients with nocturnal hyperkinetic non-REM sleep-associated seizures was temporal located as often as frontal. In these formerly presented cases, all reported incidents of ictal nightmare-like attacks were associated with localized epileptic discharges as recorded by EEG in these studies.

This phenomenon of ictal nightmare-like symptoms during non-REM sleep stages 1–2 is also observed in our patient, whereas in the case study of Silvestri et al. [23], only two adolescent patients showed ictal nightmare-like episodes out of sleep stages 3–4 (N3). This phenomenon is noteworthy because only for REM sleep was an activation of the limbic structures documented [7, 19]. However, a localized increase of metabolic activity in some areas of the temporal lobe is reported in REM and in non-REM sleep (in summary see 11). Therefore, it could be assumed that this local activation functions as a possible ictal promoting factor, if an epileptic temporal area exists. In addition, fear is an ictal symptom of seizures generated in the mesial temporal lobe [18], which is strongly connected to limbic structures. In REM sleep, a global metabolic increase excluding the prefrontal cortex is described [20]. Therefore, besides exciting circuits, also inhibiting neuronal networks could be stimulated so that the risk of ictal events in REM sleep is reduced. Another possible explanation for the notation that seizures are dominantly occurring in non-REM sleep can be found in the reports that epilepsy patients show an increase of stage 1 and stage 2 non-REM sleep (N1, N2) [6]. In addition, it is well known that drowsiness and non-REM sleep facilitate the synchronization and propagation of neuronal activity and epileptic discharges, whereas in REM sleep electroencephalographic activity is desynchronized [5]. Such a transient desynchronization is documented to be involved in orbitofrontal cortex and amygdale network activities resulting in epileptic seizures with strong emotional expressions [2, 3]. Therefore, sleep-associated nightmare-like ictal paroxysm could be generated at frontal and temporal origins, with fast spreading in a large cortical network [22]. However, in total, only some cases of ictal fearful nightmares are reported in adolescents. With respect to the history of our patient presenting symptoms 2 weeks after visiting a ski camp, premature psychological conclusions should be avoided if recurrent attacks or occurring nightmares show a highly stereotypical course and content [11].

Another interesting aspect of our case study is the unusual ictal EEG feature. In most cases reported so far, ictal EEG of temporal lobe seizures presented by nightmare-like events showed a localized spike or spike–slow wave activity. In our case, at first, scalp EEG could not document a clear localization, which is not unusual for frontal lobe epilepsy [26] although in a vast majority of cases of temporal lobe epilepsy, an accurate localization seems to be possible [24]. In addition, ictal alpha rhythms are unusual in temporal lobe epilepsy [17]. Therefore, with respect to the semiology (fear simultaneous

with dystonic hand movements, shouting and other hypermotor components, and nocturnal predominance) and the EEG features (interictal and ictal), a frontal origin of the seizures has to be discussed, although hyperkinetic and affective features of a seizure which are suggestive for frontal seizures, could occur also if the seizure is induced in a temporal zone [2]. After epigastric aura, anxiety, fear, and panic are the second-most frequent ictal subjective symptoms of temporal lobe seizures occurring in 10–35% of cases [8]. PET is a useful functional neuroimaging technique to identify the focal epileptogenic onset zone [16]. In context of the PET findings, nonlesional left temporal epilepsy is suggested in our case. To our knowledge, generalized alpha rhythms with regular spatial organization with bilateral synchronic decrease of the amplitude from occipital to frontal leads associated with semiology of fearful dreams have not yet been reported in this kind of seizure. The monomorphic generalized alpha rhythm may result from very fast secondary bilateral synchrony and may have been promoted by the global decrease of neuronal activity in non-REM sleep in combination with a higher grade of synchronization [10].

Lamotrigine is a well-established anticonvulsive drug in generalized [21] and focal epilepsy [15]. With respect to the age and gender of the patient, Lamotrigine was chosen as the first antiepileptic drug. In addition, in an earlier reported case with generalized rhythmic alpha activity as an EEG feature of the seizure, the patient became seizure-free after treatment with Lamotrigine. The authors speculated that Lamotrigine influences thalamic Ca^{+} channels thus resulting in a decrease of generalized epileptic activity [4]. Also, an involvement of subcortical structures in nocturnal non-REM sleep-associated seizures has to be taken into account [25].

In conclusion, the reported case demonstrates first, that in case of stereotypical nightmare-like episodes in adolescents, an epileptic origin has to be ruled out before a psychological discussion is started. Second, a failure to document localized discharges in scalp EEG during the seizure does not rule out a focally generated, fast-spreading epileptic activity. Third, that Lamotrigine can be effective in cases of focal temporal lobe seizures with very fast-spreading of epileptic activity, electrophysiologically imitating a primary generalized epilepsy.

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